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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/995,529	11/26/2001	Jeffry D. Watkins	P-IX 4976	2007

EXAMINER
RAWLINGS, STEPHEN L

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/995,529	WATKINS ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22 and 42-63* is/are pending in the application.

4a) Of the above claim(s) *4-16,18,19 and 44-63* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,17,21,22,42 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-22 and 42-63* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 7.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *20040419*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The election with traverse filed December 22, 2003 is acknowledged and has been entered. However, as explained in the attached Interview Summary of April 19, 2004, the response to the restriction requirement set forth in the Office action mailed October 21, 2003 is nonresponsive; nonetheless, during the interview Applicant agreed to make a provisional election, which is both responsive to the restriction requirement set forth in the Office action mailed October 21, 2003 and which is responsive to the further restriction requirement set forth below.

2. The amendment filed December 22, 2003 is acknowledged and has been entered. Claims 23-41 and 64-83 have been canceled.

3. Claims 1-22 and 42-63 are pending in the application. Claims 4-16, 18, 19, and 44-63 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention or species of invention, there being no allowable generic or linking claim.

4. Claims 1, 2, 17, 21, 22, 42, and 43, insofar as the claims are drawn to the elected species of invention, are currently under prosecution.

Election/Restrictions

5. This application contains claims directed to the following patentably distinct species of the claimed invention; accordingly, claims 1, 2, 21, 22, 44, 45, 48, 49, 51, 52, 55, 56, 58, 59, 61, and 62 are further subject to a restriction to one of the encompassed patentably distinct species of invention. Presently, claims 1, 2, 21, 22, 44, 45, 48, 49, 51, 52, 55, 56, 58, 59, 61, and 62 are generic to a plurality of disclosed patentably distinct species of invention wherein said antibody is selected from the group consisting of the disclosed antibodies that bind specifically to a cryptic collagen epitope.

Each species of antibody encompassed by the generic claims is distinct from the others because each antibody comprises unique amino acid sequences. Therefore, each species of antibody is a different product requiring a unique search that is not required of any of the other species. The search of any single species will not provide adequate information regarding any of the other species. Therefore, to the extent that the claims in each of the groups of claims, as set forth in the restriction of the Office action mailed October 21, 2003, are drawn to any one species of antibody encompassed by the generic claims within those groups, the claims are drawn to patentably distinct species of invention.

Accordingly, Applicant is required under 35 U.S.C. 121 to specifically elect a single disclosed species of invention by specifically identifying a single disclosed species of antibody that binds a cryptic collagen epitope to which the claims of the elected group will be drawn for prosecution on the merits and to which the claims shall be restricted if no generic claim is finally held to be allowable. The Examiner notes that a generic claim encompassing a novel and nonobvious species of invention may be allowable over the prior art, but not necessarily over 35 U.S.C. §§ 101 and 112.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, Applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, Applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should Applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over

the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

6. During a telephone conversation with Deborah L. Cadena on April 19, 2004, a provisional election was made with traverse to prosecute the invention of claims 1-22 and 42, insofar as the claims are drawn to the species of antibody comprising SEQ ID NOs: 45, 155, 63, 157, 22, and 77. Affirmation of this election must be made by applicant in replying to this Office action. Claims 4-16, 18, 19, and 44-63 have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention or species of invention.

7. Applicant is again reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

8. Claim 43, drawn to a nucleic acid encoding the antibody of any of claims 1-41, is rejoined with claims 1-22 and 42; therefore claim 43, to the extent that the claim is drawn to the elected species of invention, has been considered together with claims 1-22 and 42.

Information Disclosure Statement

9. The information disclosure filed June 21, 2002 has been considered. An initialed copy is attached hereto.

Sequence Rules Compliance

10. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements

of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be further examined under 35 U.S.C. §§ 131 and 132.

Sequences in Figure 5A are not identified by sequence identification numbers. As explained on the attached Notice to Comply, if necessary to correct the deficiency, Applicant is required to submit substitute copies of the sequence listing and a statement that both copies are the same and include no new matter.

Applicant is given the same period of time within which to reply to this Office action to comply with the sequence rules under 37 C.F.R. §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g).

Specification

11. The specification is objected to because of the recitation: "(see Xu et al., Hybridoma 19:375-385 (2000); Xu et al., J. Cell Biol. 154:1069-1079 (2001) [...], *each of which is incorporated herein by reference*" (italicized for emphasis) (page 19, lines 11-14). MPEP § 608.01(p) does not provide for the incorporation by reference of essential material by reference to non-patent publications. "Essential material" is defined as "that which is necessary to (1) describe the claimed invention, (2) provide an enabling disclosure of the claimed invention, or (3) describe the best mode (35 U.S.C. 112)". As a description of the monoclonal antibody HUI77 is essential, the attempt to incorporate such material by reference to the non-patent literature of Xu et al. is improper. Amending the specification to remove the incorporation by reference statement to the extent that it refers to the non-patent literature of Xu et al. can obviate this issue. Alternatively, Applicant is required to amend the specification to actually include the material incorporated by reference; and the amendment must be accompanied by an affidavit or declaration executed by Applicant, or a practitioner representing Applicant, stating that the amendatory material consists of the same material incorporated by

reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

12. The specification is objected to because the use of numerous improperly demarcated trademarks has been noted in this application. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

Examples of improperly demarcated trademarks include BIACORE (page 57, line 17, and page 65, line 7) and NeutrAvidin™ (page 86, line 6).

Appropriate corrections are required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at http://www.uspto.gov/web/menu/search.html.

13. The specification is objected to because of the following informalities: At pages 25-27, there are numerous disclosures, which appear to be typographical errors; see, e.g., "fG" at page 25, line 23. Since the disclosures appear to be indicative of an amino acid substitution at a particular position in the exemplary CDRs of a parental antibody, it is suggested "fG" should read "G", which is the single letter code for the amino acid methionine. The designations, e.g., "fG", "eM", and "eS", which are recited at pages 25-27, are unfamiliar designations for amino acid residues. Appropriate correction or explanation is required.

Claim Objections

14. Claim 17 is objected to because the claim recites, "[t]he antibody of claim 2, wherein said antibody, or functional fragment thereof, comprises [...]". Claim 2 is drawn

to an antibody or a functional fragment thereof. Therefore, if claim 17 is intended to further limit both the antibody and the functional fragment thereof, claim 17 would more properly recite, "[t]he antibody, or functional fragment thereof, of claim 2, which antibody and functional fragment comprises [...]".

15. Claim 42 is objected to because the claim recites, "[t]he grafted antibody of any one of claims 1-41, wherein said functional fragment is [...]". Claims 1, 2, 21, and 22 are drawn to a grafted antibody or functional fragment thereof. Accordingly, the grafted antibody of any of claims 1-41 is not a functional fragment thereof; rather, it's a functional fragment of the grafted antibody. Because claim 42 limits the functional fragment of the grafted antibody, claim 42 would more properly recite, "[t]he functional fragment of any of claims 1-22, wherein the functional fragment is [...]".

Claim Rejections – 35 USC § 112

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 1, 2, 17, 21, and 22, and claims 42 and 43, insofar as the claims are drawn to the antibody of any of claims 1, 2, 17, 21, and 22, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a genus of grafted antibodies and functional fragments thereof, the members of which have specific binding activity for "a cryptic collagen epitope".

The specification does not describe with any degree of particularity a single member of the genus of "cryptic collagen epitopes" to which the members of the

claimed genus of antibodies must bind, such that the specification might reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed. At page 16, lines 9-13, the specification describes "a cryptic collagen site" or "a cryptic collagen epitope'" as "an epitope of a collagen molecule that is less accessible to binding of an antibody, or functional fragment thereof, in native collagen than in denatured collagen". However, given this definition of "a cryptic collagen epitope", one skilled in the art could not immediately recognize or distinguish members of the genus of claimed antibodies capable of binding such an epitope, because one could not immediately recognize or distinguish members of the genus of cryptic collagen epitopes to which the members of the claimed genus of antibodies must bind.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it, or, by analogy, a potential method for screening for it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description'' Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by

disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

As evidenced by Greenspan et al. (*Nature Biotechnology* **7**: 936-937, 1999), defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destablilizing to binding. Furthermore, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows the epitope to which any given antibody binds can only be identified empirically. Even using a competition assay, the skilled artisan cannot determine whether an antibody binds the same epitope as another antibody because an antibody that competes with another does not necessarily bind the same epitope as the other; rather, one antibody may bind a spatially overlapping epitope to sterically hinder binding of the other.

Although claim 17 is drawn to a genus of antibodies or functional fragments thereof comprising six complementarity determining regions (CDRs) of an antibody

known to bind collagen, as noted above, the specification does not describe the "epitope" to which the members of the genus encompassed by claim 17 bind. Even relatively small changes in the structure of the antibody can change the way in which an antibody binds an antigen; such small changes thus alter the "epitope" to which an antibody binds.

Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus of epitopes to which the members of the claimed genus of antibodies must bind, the skilled artisan could not immediately recognize or distinguish members of the claimed genus of antibodies. Moreover, since the specification has not identified which amino acids of the genus of epitopes of the denatured collagen molecules to which the members of the claimed genus of antibodies must bind, which are critical or essential to the binding, one skilled in the art would not recognize that Applicant had possession of the claimed invention at the time the application was filed.

18. Claims 1, 2, 21, and 22, and claims 42 and 43, insofar as the claims are drawn to the antibody of any of claims 1, 2, 21, and 22, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making a grafted antibody, or a functional fragment thereof, antibody or functional fragment binds specifically to collagen, wherein said antibody or functional fragment comprises the three heavy chain CDRs of SEQ ID NO: 45, SEQ ID NO: 155, and SEQ ID NO: 63 and wherein said antibody or functional fragment comprises the three light chain CDRs of SEQ ID NO: 157, SEQ ID NO: 22, and SEQ ID NO: 77, does not reasonably provide enablement for making a grafted antibody, or a functional fragment thereof, which antibody or functional fragment binds specifically to a cryptic collagen epitope, wherein said antibody or functional fragment comprises only one or two heavy chain CDRs or wherein said antibody or functional fragment comprises only one or two light chain CDRs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). These factors include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

Mariuzza et al (*Annu. Rev. Biophys. Biophys. Chem.* **16**: 139-159, 1987) reviews the structural basis of antigen-antibody recognition is reviewed. A naturally occurring antibody comprises two polypeptides, the so-called light and heavy chains. The antigen-combining site of an antibody is a three-dimensional structure, which fully comprises six "complementarity-determining regions" (CDRs), three each from the light and heavy chains. The amino acid sequences of the CDRs are hypervariable, as the amino acid residues contained within the CDRs determine much of antibody's antigen-binding specificity. Of the amino acid residues of the antibody contacting the antigen, six are within the light chain, nine are within the heavy chain, and two are within the constant or nearly constant "framework" regions.

The claims encompass a grafted antibody that comprises fewer than three light chain CDRs and/or fewer than three heavy chain CDRs. However, while the artisan would not expect such an antibody to bind specifically to an antigen, the specification fails to teach one to make such an antibody, which retains specific binding affinity for a cryptic collagen epitope. Accordingly, the amount of guidance, direction, and exemplification set forth by Applicant is not reasonably commensurate in scope with the claims and is not sufficient to enable the skilled artisan to make the claimed invention with a reasonable expectation of success without need of performing an additional amount of undue experimentation.

19. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

20. Claims 1, 21, 22, 42, and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 21, and 22 are indefinite because claim 1 recites, "comprising one or more complementarity determining regions (CDRs) having at least one amino acid substitution in one or more CDRs of a heavy chain CDR [...] or a light chain CDR", claim 21 recites, "comprising one or more CDRs having at least one amino acid substitution in one or more heavy chain CDRs", and claim 22 recites, "comprising one or more CDRs having at least one amino acid substitution in one or more light chain CDRs". A heavy or light chain CDR does not comprise one or more CDRs; while a heavy and light chain each comprise three CDRs, a heavy or light chain CDR is a CDR. Accordingly, the recitation renders the claims indefinite. Because the claim is indefinite, the metes and bounds of invention are not clearly delineated by the claim, which therefore fails to meet the requirements set forth under 35 USC § 112, second paragraph.

21. Claims 42 and 43 are indefinite because the claims depend from canceled claims 23-41. Therefore, the metes and bounds of claims 42 and 43 cannot be determined.

Double Patenting

22. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double

patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

23. Claims 1, 2, 17, 21, and 22, and claims 42 and 43, insofar as the claims are drawn to the antibody of any of claims 1, 2, 17, 21, and 22, are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 6, 10, 14, 16, and 17 of copending Application No. 09/478,977. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons:

Claims 1-4, 6, 10, 14, 16, and 17 of the copending application are drawn to an antagonist that specifically binds to a denatured collagen or collagens but binds to the native triple helical form of each of said collagens with substantially reduced affinity, which antagonist inhibits angiogenesis, wherein said antagonist is a humanized or chemically modified monoclonal antibody or a fragment thereof and wherein said reduced affinity is about 3, 5, or 10 fold lower than for said denatured collagen. Instant claims 1, 2, 21, and 22 are drawn to a grafted monoclonal antibody, i.e., a humanized or chemically modified monoclonal antibody, or a functional fragment thereof, comprising a heavy chain CDR1 referenced as SEQ ID NO: 45, a heavy chain CDR2 referenced as SEQ ID NO: 155, a heavy chain CDR3 referenced as SEQ ID NO: 63, a light chain CDR1 referenced as SEQ ID NO: 157, a light chain CDR2 referenced as SEQ ID NO: 22, and a light chain CDR3 referenced as SEQ ID NO: 77. The properties of the antibody claimed in the instant application, which antibody comprises a heavy chain CDR1 referenced as SEQ ID NO: 45, a heavy chain CDR2 referenced as SEQ ID NO: 155, a heavy chain CDR3 referenced as SEQ ID NO: 63, a light chain CDR1 referenced as SEQ ID NO: 157, a light chain CDR2 referenced as SEQ ID NO: 22, and a light chain CDR3 referenced as SEQ ID NO: 77, are inherent properties of the antibody. The instant specification teaches the disclosed antibody of claims 1, 2, 21, and 22, which

comprises a heavy chain CDR1 referenced as SEQ ID NO: 45, a heavy chain CDR2 referenced as SEQ ID NO: 155, a heavy chain CDR3 referenced as SEQ ID NO: 63, a light chain CDR1 referenced as SEQ ID NO: 157, a light chain CDR2 referenced as SEQ ID NO: 22, and a light chain CDR3 referenced as SEQ ID NO: 77, binds a denatured collagen or collagens but binds to the native triple helical form of each of said collagens with substantially reduced affinity and is capable of inhibiting angiogenesis; see, e.g., page 3, lines 3-5, page 16, lines 9-28, and claim 48 of the instant application. Therefore, since the claims of the instant application are drawn to a species of antibody, which is encompassed by the more generic claims of the copending application, even though the conflicting claims are not identical, they are not patentably distinct from each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

24. No claims are allowed.

25. The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure. WO 00/40597 A1, Xu et al. (*Hybridoma* **19**: 375-385, 2000), Wheatcroft et al. (*Matrix Biol.* **18**: 361-372, 1999), Kalluri et al. (*Proc. Assoc. Am. Physicians* **108**: 134-139, 1996), Borza et al. (*J. Biol. Chem.* **275**: 6030-6037, 2000), Nakanishi et al. (*Kidney Int.* **46**: 1413-1421, 1994), Yoshioka et al. (*Am. J. Pathol.* **144**: 986-996, 1994), and David et al. (*J. Biol. Chem.* **276**: 6370-6377, 2001) each teach an antibody, which binds a cryptic collagen epitope. Yang et al. (*J. Mol. Biol.* **254**: 392-403, 1995) teach affinity maturation of an antibody.

26. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne (Bonnie) Eyler, Ph.D. can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
April 21, 2004

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600